

Digoxin

jako bradykardizující lék

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Česká asociace srdečního selhání Bradykardizující
léčba srdečního selhání ve spolupráci s PS
Kardiovaskulární farmakoterapie
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William Withering

1741-1799

✍ It is much easier to write upon a disease than upon a remedy.

😊 The former is in the hands of Nature and a faithful observer with an eye of tolerable judgement cannot fail to delineate a likeness.

☹ **The latter will ever be subject to the whin, the inaccuracies and the blunder of mankind.**

AN
ACCOUNT OF THE FOXGLOVE,
AND
Some of its Medical Uses:
with
PRACTICAL REMARKS ON DROPSY,
AND OTHER DISEASES.

By
WILLIAM WITHERING, M. D.
Physician to the General Hospital at Birmingham.

nonumque prematur in annum.
Horace.

BIRMINGHAM: PRINTED BY M. SWINNEY;
FOR C.G.J. AND J. ROBINSON, PATERNOSTER ROW, LONDON.
MDCCLXXXV

- 👉 „Mother Hutton“ byla bylinkářka a léčitelka z Shropshire, která používala tajnou rodinnou směs 20 bylin k léčbě otoků...jednou z nich byl i digitalis
- 👉 W. Withering ji přesvědčil, aby mu prozradila recepturu a odhalil, že aktivní substancí byl digitalis
- 👉 V roce 1785 popsal 163 případů léčby tímto preparátem
- 👉 O přínosu Mrs Hutton se ovšem nikdy nezmínil...

William Withering

The foxglove's leaves, with caution given,
Another proof of favouring Heav'n
Will happily display;
The rapid pulse it can abate;
The hectic flush can moderate
And, blest by Him whose will is fate,
May give a lengthen'd day.

Listy náprstníku s opatrností podané
Šťastně poskytují další důkaz
blahodárné Vůle Nebes:
Rychlý tep mohou zklidnit
Hektický flush mohou zmírnit
A s požehnáním Toho, jehož vůle je osudem
Mohou dát i prodloužený den

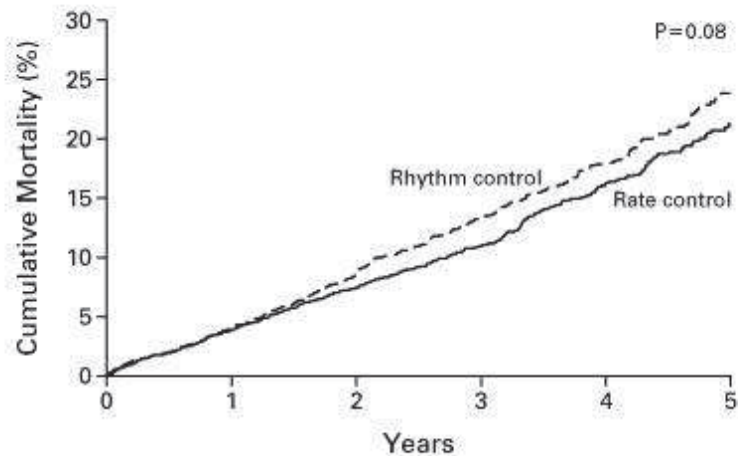
2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: Executive Summary

- 👉 Digoxin is effective to control resting heart rate with HFrEF **I C**
- 👉 Digoxin is effective to control resting heart rate in patients with HF with reduced ejection fraction. **I B**
- 👉 A combination of digoxin and a beta blocker (or a nondihydropyridine calcium channel antagonist for patients with HFpEF) is reasonable to control resting and exercise heart rate in patients with AF **IIaB.**

Digoxin a fibrilace síní

Studie AFFIRM

DRUG	RATE-CONTROL GROUP		RHYTHM-CONTROL GROUP	
	USED DRUG FOR INITIAL THERAPY	USED DRUG AT ANY TIME	USED DRUG FOR INITIAL THERAPY	USED DRUG AT ANY TIME
	no. of patients (%)			
Rate control				
Data available	1957	2027	1266	2033
<u>Digoxin</u>	949 (48.5)	1432 (70.6)	417 (32.9)	1106 (54.4)
Beta-blocker	915 (46.8)	1380 (68.1)	276 (21.8)	1008 (49.6)
Diltiazem	583 (29.8)	935 (46.1)	198 (15.6)	610 (30.0)
Verapamil	187 (9.6)	340 (16.8)	56 (4.4)	204 (10.0)

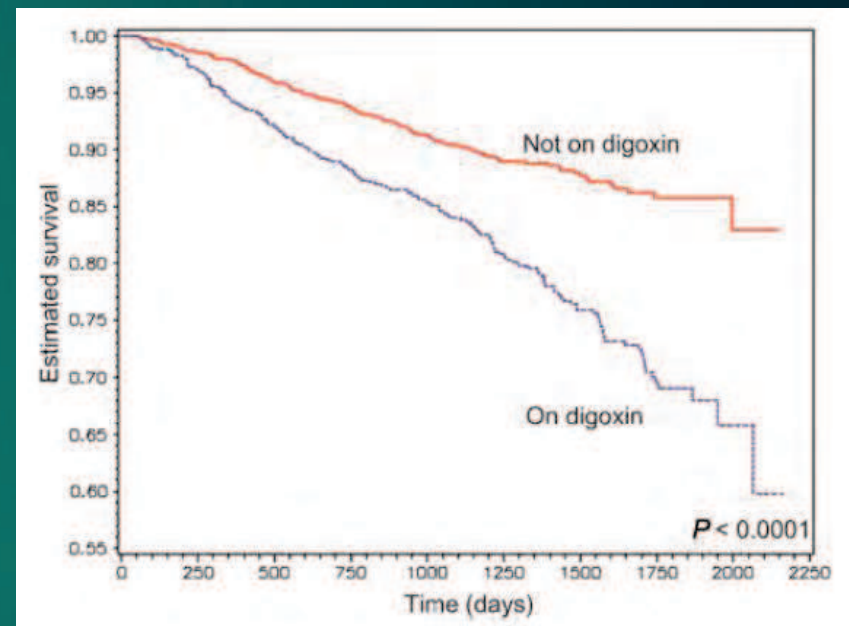


No. of DEATHS	number (percent)					
	0	1	2	3	4	
Rhythm control	0	80 (4)	175 (9)	257 (13)	314 (18)	352 (24)
Rate control	0	78 (4)	148 (7)	210 (11)	275 (16)	306 (21)

Digoxin a fibrilace síní

Increased mortality among patients taking digoxin—analysis from the AFFIRM study

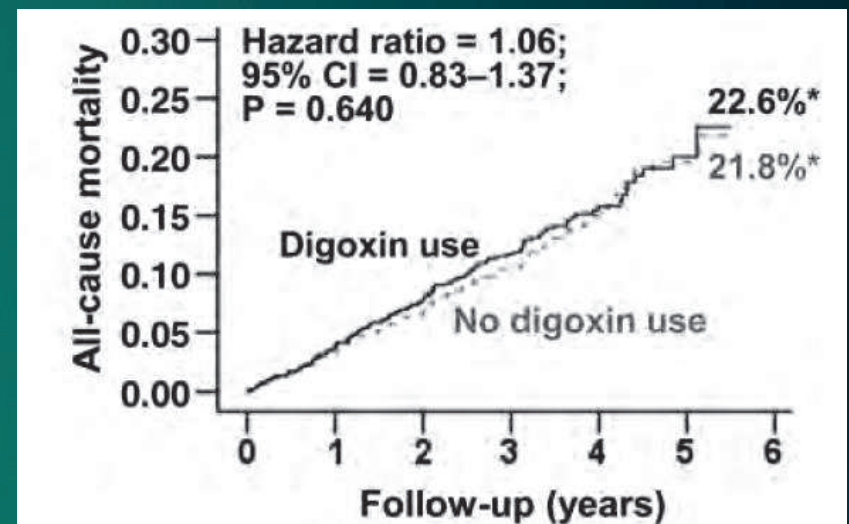
Among patients with AF enrolled in the AFFIRM trial, digoxin was associated with increased all-cause mortality, CV mortality, and arrhythmic deaths in a propensity-adjusted analysis that controlled for multiple comorbidities. The increase in all-cause mortality was consistently observed in men and women and in patients with and without underlying HF. Our study underscores the importance of reassessing the role of digoxin in the contemporary management of AF in patients with or without HF.



Digoxin a fibrilace síní

Lack of evidence of increased mortality among patients with atrial fibrillation taking digoxin:

In patients with paroxysmal and persistent AF enrolled in the AFFIRM trial, we found no evidence of an increased risk of mortality or hospitalization among those receiving digoxin for rate control, either as monotherapy or in combination with other rate-control drugs. These findings do not support the recent suggestion that the use of digoxin in AF should be questioned nor support that there is a need to reassess the role of digoxin in the management of AF in patients with and without HF.



Digoxin a fibrilace síní

When 'digoxin use' is not the same as 'digoxin use': lessons from the AFFIRM trial

Sabina A. Murphy*

	Whitbeck et al.	Gheorghiade et al.
Study design	Non-randomized, observational analysis using data from randomized AFFIRM trial	Non-randomized, observational analysis using data from randomized AFFIRM trial
Time point digoxin used assessed	Time-varying covariate, throughout study	Fixed, at baseline only
Cohort	Full cohort ($n = 4058$)	Selected cohort ($n = 1756$)
Propensity method	Adjustment	Matching ^a
Primary HR for digoxin and all-cause mortality association	HR 1.41, 95% CI 1.19–1.67; $P < 0.001$	HR 1.06, 95% CI 0.83–1.37; $P = 0.640$
Main conclusion from authors	Digoxin associated with significant increase in all-cause mortality in patients with AF	No evidence of increased mortality associated with digoxin use as baseline initial therapy in patients with AF

Digoxin a fibrilace síní

When 'digoxin use' is not the same as 'digoxin use': lessons from the AFFIRM trial

Sabina A. Murphy*

- 👉 Interpretace jedné a téže studie přineslo zcela rozdílné výsledky
- 👉 Jde o retrospektivní hodnocení
- 👉 Ani sofistikované metody, jako je propenzity analýza nemohou nahradit dvojitou slepou randomizaci.
- 👉 Není jasné, co stojí za zvýšením celkové mortality
- 👉 Význam „statistických her“

Increased Mortality Associated With Digoxin in Contemporary Patients With Atrial Fibrillation

Findings From the TREAT-AF Study

PHASE 1: IDENTIFYING 122,465 STUDY COHORTS

Initial criteria:

Patients included if they met the following:

- Newly diagnosed Atrial Fibrillation/Atrial Flutter (AF)
- In U.S. Department of Veterans Affairs Health Care System (VA), between October 1, 2003 – September 30, 2008
- At least 1 primary visit and receipt of any prescriptions within 90 days after diagnosis date

Secondary criteria:

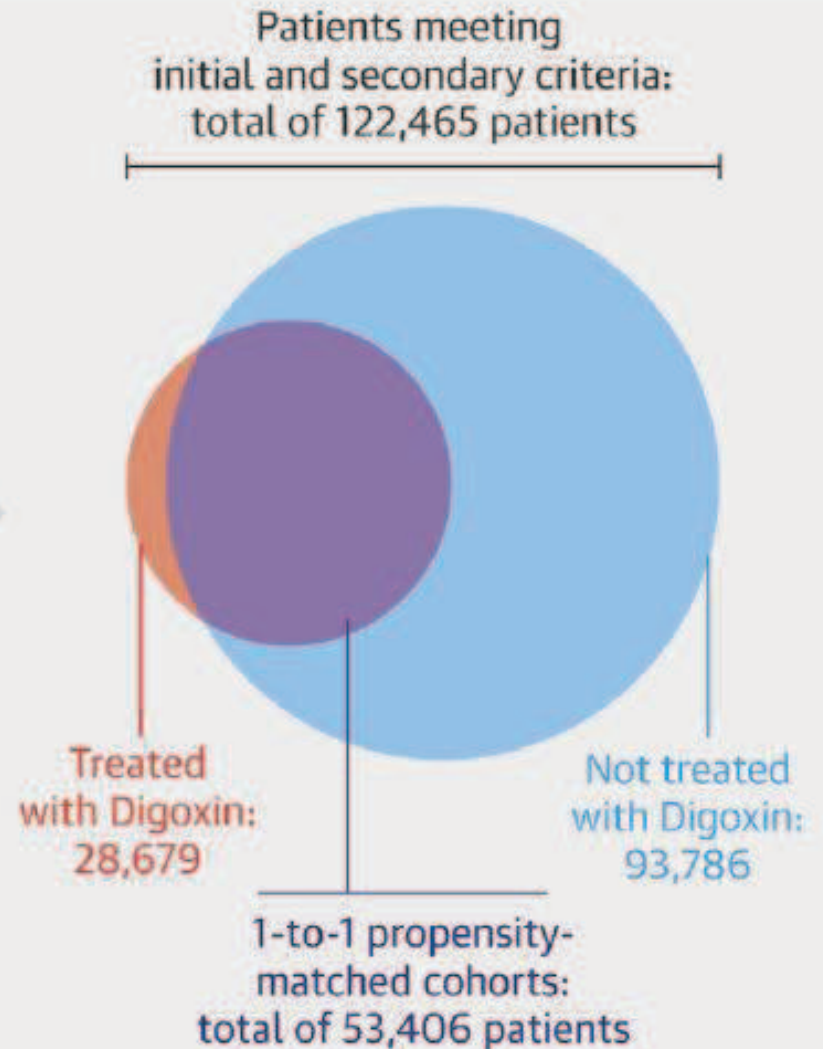
Patients excluded if they met any of the following:

- Prior AF diagnosis
- History of valve disease, repair, or replacement
- Thyroid disease
- Kidney transplant
- Cardiac surgery within 30 days

Increased Mortality Associated With Digoxin in Contemporary Patients With Atrial Fibrillation

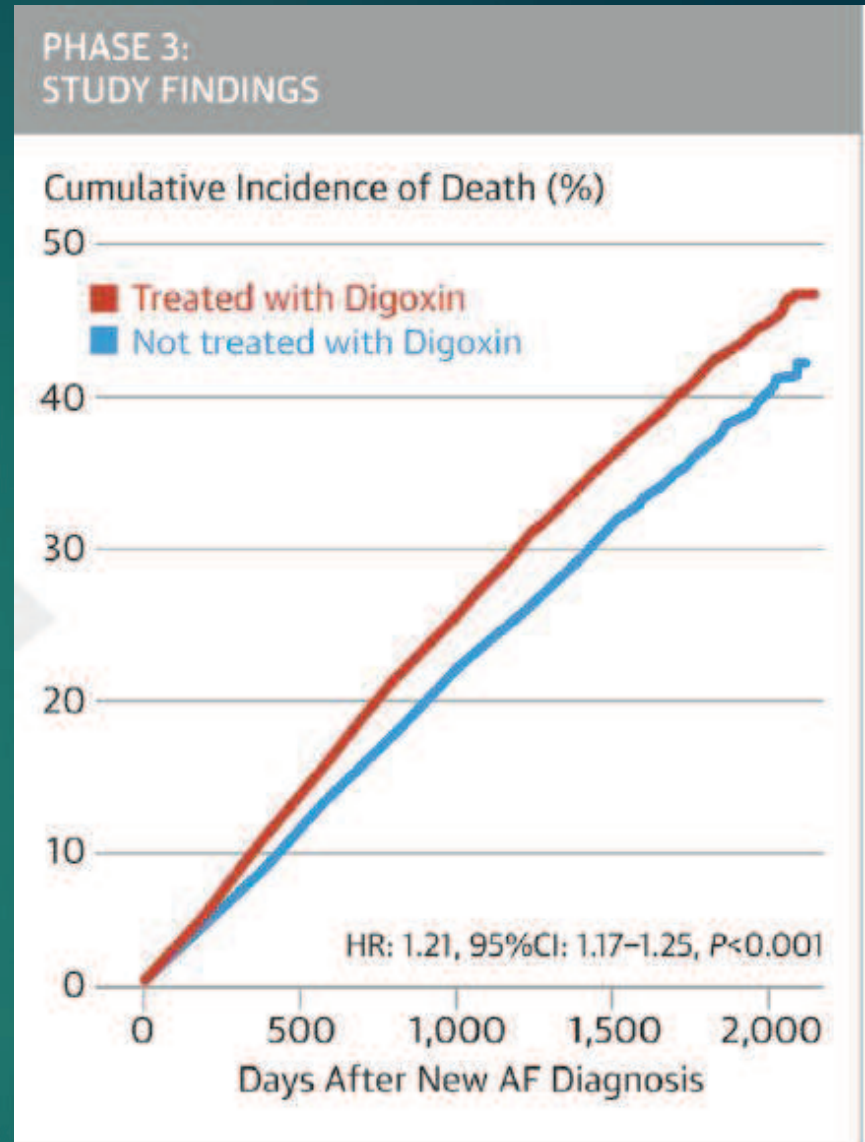
Findings From the TREAT-AF Study

PHASE 2:
NARROWING TO 53,406 STUDY COHORTS



Increased Mortality Associated With Digoxin in Contemporary Patients With Atrial Fibrillation

Findings From the TREAT-AF Study



CONCLUSIONS Digoxin was associated with increased risk of death in patients with newly diagnosed AF, independent of drug adherence, kidney function, cardiovascular comorbidities, and concomitant therapies.

EDITORIAL COMMENT

Outcomes With Digoxin in Atrial Fibrillation More Data, No Answers*

Matthew R. Reynolds, MD, MSc

The main implication of the Turakhia et al. paper and related data is that **digoxin should be used selectively and with care in AF patients**. This view is reflected in the recently updated AF treatment guidelines, where beta-blockers and non-dihydropyridine calcium channel blockers were given a Class I recommendation for rate control, and **digoxin received no specific recommendation at all**.

EDITORIAL COMMENT

Outcomes With Digoxin in Atrial Fibrillation More Data, No Answers*

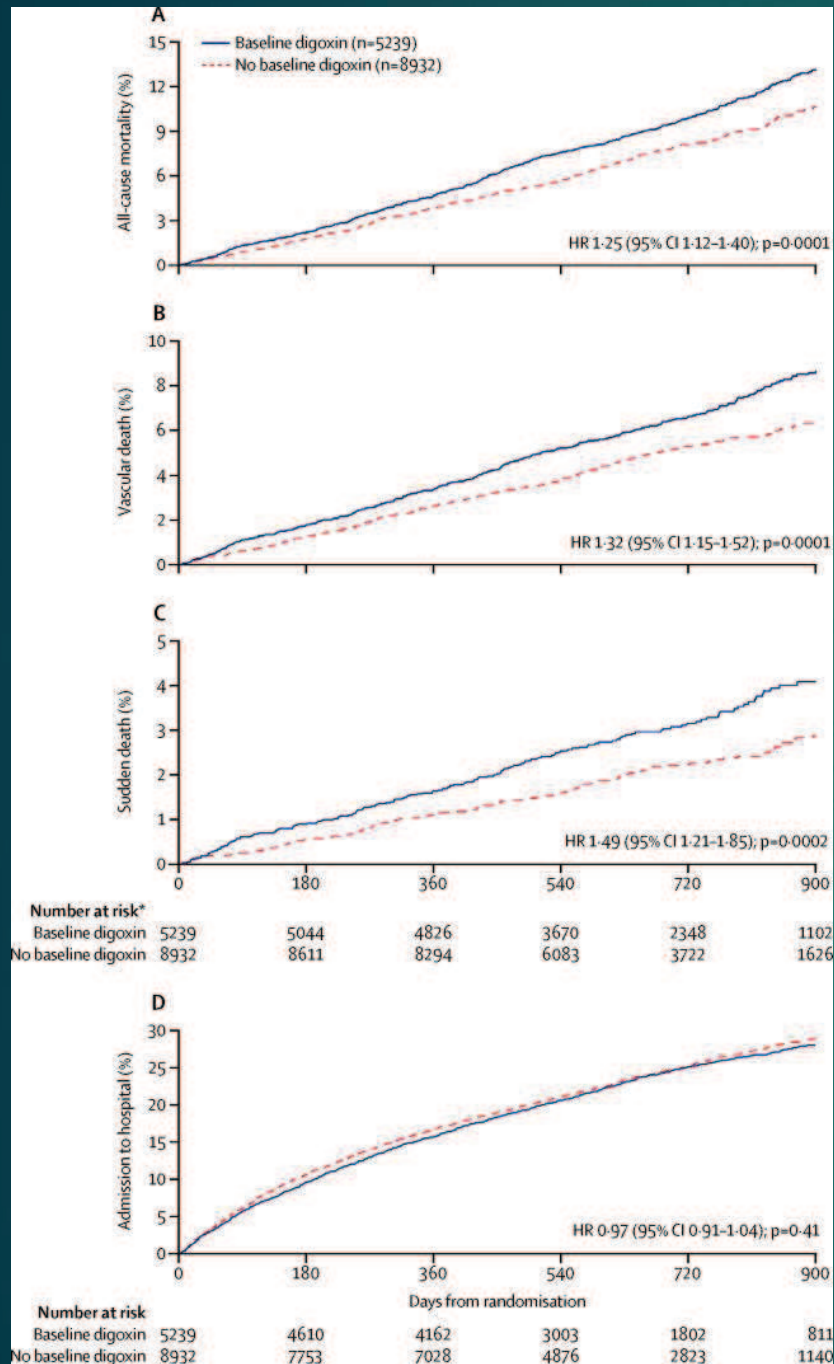
Matthew R. Reynolds, MD, MSc

Should the use of digoxin for rate control in AF be abandoned altogether? Such a recommendation cannot be made on the basis of this kind of observational data. Going forward, the role of digoxin in AF treatment may continue to diminish. **For now, there are still clinical circumstances (HF, difficult rate control, low blood pressure) where this old herbal remedy remains useful.**

Digoxin a fibrilace síní

Digoxin use in patients with atrial fibrillation and adverse cardiovascular outcomes: a retrospective analysis of the Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET AF)

- 👉 14 171 nemocných
- 👉 Retrospektivní hodnocení
- 👉 Digoxin užívalo 37% nemocných
- 👉 Více digoxin užívaly ženy, nemocní se srdečním selháním, s DM a fi si



Digoxin treatment was associated with a significant increase in all-cause mortality, vascular death, and sudden death in patients with AF. This association was independent of other measured prognostic factors, and although residual confounding could account for these results, these data show the possibility of digoxin having these effects. A randomised trial of digoxin in treatment of AF patients with and without heart failure is needed.

COMMENT

Digoxin use in atrial fibrillation: a critical reappraisal

*Sadiya S Khan, *Mihai Gheorghiu*

The available data suggest a need to redefine how digoxin is used in patients with AF. We recommend that digoxin should continue to be used in patients with AF. However, dosing should be adjusted with a goal to maintain an SDC with an upper limit of 1.0 ng/mL and not to target ventricular rate.

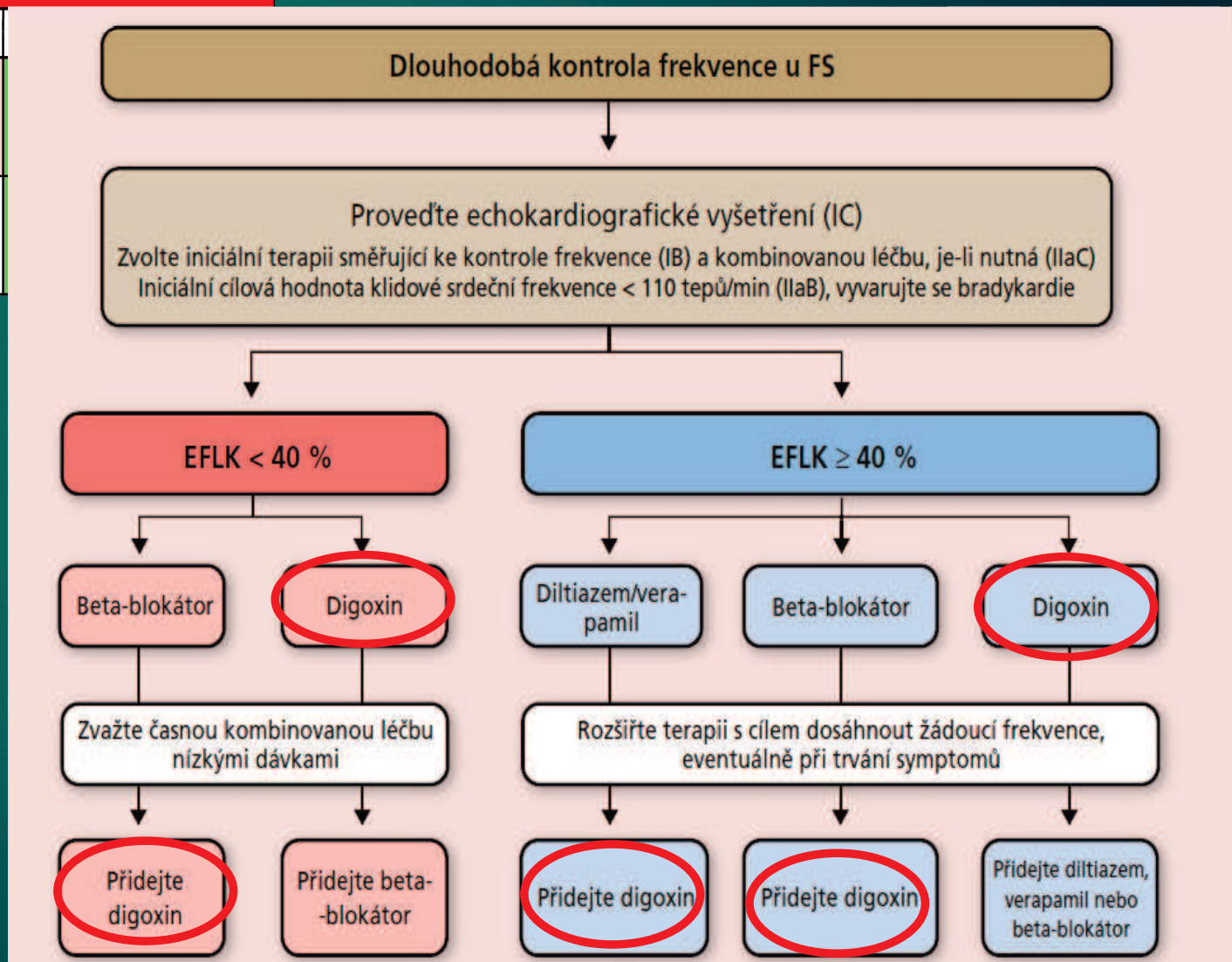
Jaká je současná role digoxinu u fibrilace síní ?

Doporučení ohledně kontroly srdeční frekvence

Doporučení

Beta-blokátory, digoxin, diltiazem nebo verapamil jsou doporučovány k dosažení kontroly frekvence u FS při EFLK ≥ 40 %.

Beta-blokátory a/nebo digoxin jsou doporučovány k dosažení kontroly frekvence u FS při EFLK < 40 %.



Digoxin – dnes IIb B

- Digoxin může být zvažován u nemocných se sin. rytmem ke snížení rizika hospitalizací u symptomatického selhání²¹
- **Pro léčbu HFrEF a FiS s rychlou odpovědí komor je pouze doporučen, když ostatní léčebné volby nemohou být použity**
- Klidová frekvence komor je doporučena 70–90/min, ačkoliv i klidová frekvence do 110/min je ještě akceptována
- Digitalis by měl vždy být předepisován za kontroly specialisty.

Pozornost vyžadují ženy, starší a nemocní se sníženými ledvinnými funkcemi